II. REMARKS

Formal Matters

Claims 1-57 are pending after entry of the amendments set forth herein.

Claims 1-29 were examined. Claims 5-11 were rejected. Claims 1-4 and 13-29 were withdrawn from consideration. Claim 12 was objected to.

Claims 5-9 and 12 are amended. The amendments to the claims were made solely in the interest of expediting prosecution, and are not to be construed as an acquiescence to any objection or rejection of any claim. Support for the amendments to claims 5-9 and 12 is found in the claims as originally filed, and throughout the specification, in particular at the following exemplary locations: claim 5: page 8, lines 5-7; and page 8, line 29 to page 9, line 1; claim 7: page 7, lines 3-9; page 10, lines 1-2; and page 10, lines 13-23; and claim 8: page 19, lines 10-12. Accordingly, no new matter is added by these amendments.

Please replace claims 5-8 and 12 with the clean version provided above.

Claims 30-57 are added. Support for new claims 30-51 is found in claims 5-12 as originally filed, and throughout the specification, including at the following exemplary locations: claims 30 and 39: page 8, lines 5-7; page 8, line 29 to page 9, line 1; and page 45, lines 27-27; claims 33 and 42: page 7, lines 3-9; page 10, lines 1-2; and page 10, lines 13-23; claim 43: page 45, line 25; claims 34 and 44: page 19, lines 10-12; claims 49, 51, and 53: page 19, lines 10-12, page 14, lines 12-13; page 18, line 28, and page 23, line 25 to page 27, line 7; claims 50, 52, and 54: page 13, line 23 to page 14, line 5; claims 55-57: page 8, line 21 to page 9, line 2. Accordingly, no new matter is added.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached is captioned "**VERSION WITH MARKINGS TO SHOW CHANGES MADE.**"

Applicants respectfully request reconsideration of the application in view of the remarks made herein.

Restriction Requirement

The Office Action stated that the restriction requirement was made final. Applicants respectfully request rejoinder of method claims 25-27 (Group VI), to the extent that these claims recite all the limitations of allowed composition claims. *In re Ochiai* 37 USPQ2d 1127 (Fed. Cir. 1995).

Objections to the specification

The Office Action objected to the specification. The Office Action stated that the specification has gaps such as those corresponding to ATCC deposit numbers. The paragraph that makes reference to ATCC deposit numbers has been deleted, thereby adequately addressing this rejection.

Objections to the claims

The Office Action objected to claims 5-12.

Claim 12

The Office Action stated that claim 12 is objected to under 37 C.F.R.§1.75(c) as being in improper form because a multiple dependent claim cannot depend from two claims simultaneously.

Applicants note that claim 12 is not a dependent claim. While claim 12 recites a method of producing a glycosyl sulfotransferase according to Claim 1, the method comprising growing a cell according to Claim 10, claim 12 does not depend from claim 1 or from claim 10. A dependent claim further limits a claim from which it depends. Claim 12 is a method claim and does not further limit claim 1 (which is directed to a nucleic acid) or claim 10 (which is directed to a cell). Accordingly, claim 12 is in proper form and need not be amended.

Claims 5-11

The Office Action stated that claims 5-11 are objected to because these claims depend from non-elected base claim 1, and suggested re-writing claim 5 as an independent claim.

Claim 5 is re-written as an independent claim, according to the suggestion in the Office Action.

Rejection under 35 U.S.C.§112, second paragraph

Claim 8 was rejected under 35 U.S.C.§112, second paragraph, as allegedly indefinite.

The Office Action stated that the term "mimetic thereof" is indefinite.

Without conceding as to the correctness of this rejection, claim 8 is amended to delete the word "mimetic."

The Office Action stated that the term "stringent conditions" in claim 8 is vague and indefinite. Applicants respectfully traverse the rejection.

Those skilled in the art are well aware of stringent hybridization conditions. Stringent hybridization conditions are amply described in standard molecular biology protocol texts. The Office Action acknowledged that the specification provides exemplary stringent hybridization conditions. Using the guidance in the specification, and the general knowledge in the art, those skilled in the art could readily prepare nucleic acids as claimed. Accordingly, this term is clear, and claim 8 need not be amended.

Nevertheless, and solely in the interest of expediting prosecution, claim 8 is amended to recite stringent hybridization conditions.

Applicants submit that the rejection of claim 8 under 35 U.S.C. §112, second paragraph has been adequately addressed in view of the remarks set forth above. The Examiner is thus respectfully requested to withdraw the rejection.

Rejection under 35 U.S.C.§112, first paragraph

Claims 5, and 7-11 were rejected under 35 U.S.C.§112, first paragraph, as allegedly lacking written description.

The Office Action stated that claims 5 and 7 are directed to genera of isolated nucleic acids and/or fragments thereof, from any source of species which have been merely defined by function as encoding glycosyl sulfotransferase GST-4α. Applicants respectfully traverse the rejection.

Comments regarding written description

The Revised Interim Guidelines for Examination of Patent Applications Under 35 U.S.C. §112, paragraph 1 "Written Description" Requirement, (*Federal Register* (Dec. 21, 1999) Vol. 64 (No. 244):71427-71440) ("Revised Guidelines"), state:

(1) "There is a strong presumption that an adequate written description of the claimed invention is present when the application is filed";

(2) the Office has the initial burden of presenting evidence or reasons why a person skilled in the art would not recognize that the written description of the invention provides support for the claims;

(3) "Consequently, rejection of an original claim for lack of written description should be rare";

(4) an Examiner should review the entire application to understand what the applicant has described as the essential features of the invention; and

(5) the Examiner's review of the application is to be conducted *from a standpoint of one of skill*

in the art at the time the application was filed and should include a determination of the field of the invention and the level of skill and knowledge in the art (emphasis added). Revised Guidelines, at page 71435.

The Office Action has not presented sufficient evidence or reasons why a person skilled in the art would not recognize that the written description of the claimed invention provides support for the claims.

As stated in the Revised Guidelines, "In most technologies which are mature, and *wherein the knowledge and level of skill in the art is high*, a written description question should not be raised for original claims even if the specification discloses only a method of making the invention and the function of the invention." Revised Guidelines, page 71436. The written description guidelines are based in part on *University of California v. Eli Lilly and Co.*, 43 USPQ2d 1398 (Fed. Cir.1997). It should be remembered that *University of California v. Eli Lilly and Co.*, (Fed. Cir.1997) was based on a patent that was filed in 1977, i.e., over 20 years ago, when the level of skill in the art was not at the level that it was as of the filing date of the instant application.

The instant specification

The instant specification provides the nucleotide sequences of mouse and human GST-4, including human GST-4α and GST-4β, which sequences are highly related and which encode enzymes having glycosyl sulfotransferase activity. The instant specification further provides the nucleotide sequences of mouse and human GST-6. The specification provides the sequences of: (1) mouse GST-4 cDNA; (2) human GST-4α cDNA; (3) human GST-4β cDNA, as well as human genomic GST-4α DNA and human genomic GST-4β DNA; (4) mouse GST-6 cDNA; (5) mouse GST-6 genomic DNA; (6) human GST-6 cDNA; and (7) human GST-6 genomic DNA. Thus, the specification provides the sequences of three different cDNAs and two genomic DNAs encoding GST-4 (including GST-4α and GST-4β), as well as two different cDNAs and two genomic DNAs encoding GST-6. Applicants submit that a description of five different cDNAs from two different species is sufficient to satisfy the written description requirement of 35 U.S.C.§112, first paragraph.

Furthermore, the Office Action is required to review the application *from a standpoint of one of skill in the art at the time the application was filed and should include a determination of the field of the invention and the level of skill and knowledge in the art*, as set forth in the written description guidelines. The level of skill and knowledge in the art is such that those in the field would recognize that a

description of three different GST-4 cDNAs and two different GST-6 cDNAs from two different species is evidence that Applicants had possession of the claimed invention at the time of filing.

Nevertheless, and solely in the interest of expediting prosecution, claim 7 is amended to recite fragments that catalyze the transfer of a sulfate group from a donor to a selectin ligand; and claim 5 is amended to recite that the nucleic acid has a nucleotide sequence that encodes a GST-4α polypeptide having at least 85% amino acid sequence identity to the amino acid sequence set forth in SEQ ID NO:08.

Applicants submit that the rejection of claims 5, and 7-11 under 35 U.S.C. §112, first paragraph, has been adequately addressed in view of the remarks set forth above. The Examiner is thus respectfully requested to withdraw the rejection.

Rejection under 35 U.S.C.§102(e)

Claims 5, 6, and 8-11 were rejected under 35 U.S.C.§102(e) as allegedly anticipated by Bistrup et al. (U.S. Patent No. 6,265,192; hereinafter "Bistrup").

The Office Action stated that Bistrup teaches an isolated DNA sequence that has glycosyl sulfotransferase function, and further stated that since the functional differences between glycosyl transferase of the instant invention and that of Bistrup are not clear, it is reasonable to conclude that Bistrup meets the limitations of claim 5. Applicants respectfully traverse the rejection.

Claim 5 as amended recites a nucleic acid that has a nucleotide sequence that encodes a GST-4α polypeptide that has comprises an amino acid sequence that is at least 85% identical to the amino acid sequence set forth in SEQ ID NO:08. Bistrup does not disclose such a nucleic acid. Furthermore, Bistrup does not disclose or suggest a nucleic acid that encodes a GST polypeptide comprising an amino acid sequence having at least 85% amino acid sequence identity to the amino acid sequence set forth in SEQ ID NO:13 (human GST-4β). Bistrup does not disclose or suggest a nucleic acid that encodes a GST polypeptide comprising an amino acid sequence having at least 85% amino acid sequence identity to SEQ ID NO:15 (human GST-6 cDNA). Accordingly, Bistrup cannot anticipate claim 5, or claims 6 and 8-11, which depend, directly or indirectly, from claim 5.

Applicants submit that the rejection of claims 5, 6, and 8-11 under 35 U.S.C. §102(e) has been adequately addressed in view of the remarks set forth above. The Examiner is thus respectfully requested to withdraw the rejection.

Rejection under 35 U.S.C.§102(a)

Claims 5, 6, and 8-11 were rejected under 35 U.S.C.§102(a) as allegedly anticipated by Lee et al. ((1999) *Biochem. Biophys. Res. Comm.* 263:543-549; hereinafter "Lee").

The Office Action stated that Lee teaches an isolated DNA sequence encoding human GST-4α which has 100% identity to SEQ ID NO:1. Applicants respectfully traverse the rejection.

Lee is not available as prior art to the instant application. The instant application claims the benefit of the filing date of U.S. Provisional Patent Application No. 60/144,694, which was filed on July 20, 1999. Lee was published after July 20, 1999 (indeed, Lee was not received by the journal until August 13, 1999), and as such is not available as prior art to the instant application.

Applicants submit that the rejection of claims 5, 6, and 8-11 under 35 U.S.C. §102(a) has been adequately addressed in view of the remarks set forth above. The Examiner is thus respectfully requested to withdraw the rejection.

Rejection under 35 U.S.C.§102(b)

Claims 5 and 7-11 were rejected under 35 U.S.C.§102(b) as allegedly anticipated by Fukuta et al. ((1997) *J. Biol. Chem.* 272:32321-32328; hereinafter "Fukuta").

The Office Action stated that Fukuta teaches an isolated DNA sequence encoding human sulfate Gal-6-sulfotransferase, and that no structural limitation of the nucleic acid recited in claim 5 is provided. The Office Action stated that since the specific and exact differences between the function of Fukuta's sulfotransferase and the GST-4α of the instant invention are not clear, Fukuta's DNA sequence meets the limitations of claims 5 and 8. Applicants respectfully traverse the rejection.

Claim 5 as amended recites a nucleic acid that has a nucleotide sequence that encodes a GST-4α polypeptide that has comprises an amino acid sequence that is at least 85% identical to the amino acid sequence set forth in SEQ ID NO:08. Fukuta does not disclose such a nucleic acid. Furthermore, Fukuta does not disclose or suggest a nucleic acid that encodes a GST polypeptide comprising an amino acid sequence having at least 85% amino acid sequence identity to the amino acid sequence set forth in SEQ ID NO:13 (human GST-4β). Fukuta does not disclose or suggest a nucleic acid that encodes a

GST polypeptide comprising an amino acid sequence having at least 85% amino acid sequence identity to SEQ ID NO:15 (human GST-6 cDNA). Accordingly, Fukuta cannot anticipate claim 5, or claims 6 and 8-11, which depend, directly or indirectly, from claim 5.

Applicants submit that the rejection of claims 5 and 7-11 under 35 U.S.C. §102(b) has been adequately addressed in view of the remarks set forth above. The Examiner is thus respectfully requested to withdraw the rejection.

III. CONCLUSION

Applicants submit that all of the claims are in condition for allowance, which action is requested. If the Examiner finds that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-0815, order number UCAL-138.

Respectfully submitted,
BOZICEVIC, FIELD & FRANCIS LLP

Date: June 27, 2002

By: _____

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE SPECIFICATION

On page 1, after the title, please insert the following text:

-- CROSS REFERENCE TO RELATED APPLICATIONS

This application claims the benefit of U.S. Provisional Patent Application No. 60/14,694, filed July 20, 1999, which application is incorporated by reference herein in its entirety. --

Please delete the paragraph beginning on page 12, line 9, as follows:

[SEQ ID Nos:1, 10, 11, 12, 18, and 19 have been deposited with the American Type Culture Collection and are available under accession numbers _____, respectively.]

Please enter the amendments to the paragraph beginning on page 36, line 3, as follows:

Among useful changes in the backbone chemistry are phosphorothioates; phosphorodithioates, where both of the non-bridging oxygens are substituted with sulfur; phosphoroamidites; alkyl phosphotriesters and boranophosphates. Achiral phosphate derivatives include 3'-O'-5'-S-phosphorothioate, 3'-S-5'-O-phosphorothioate, 3'-CH2-5'-O-phosphonate and 3'-NH-5'-O-phosphoroamidate. Peptide nucleic acids replace the entire ribose phosphodiester backbone with a peptide linkage. Sugar modifications are also used to enhance stability and affinity. The [□-anomer] α-anomer of deoxyribose may be used, where the base is inverted with respect to the natural [□-anomer] β-anomer. The 2'-OH of the ribose sugar may be altered to form 2'-O-methyl or 2'-O-allyl sugars, which provides resistance to degradation without comprising affinity. Modification of the heterocyclic bases must maintain proper base pairing. Some useful substitutions include deoxyuridine for deoxythymidine; 5-methyl-2'-deoxycytidine and 5-bromo-2'-deoxycytidine for deoxycytidine. 5-propynyl-2'-deoxyuridine and 5-propynyl-2'-deoxycytidine have been shown to increase affinity and biological activity when substituted for deoxythymidine and deoxycytidine, respectively.

Please enter the amendments to the paragraph beginning on page 43, line 29 to page 44, line 29, as follows.

Further examination of the H4 contig revealed that a long open reading frame encoding a novel member of the galactose/GlcNAc/GalNAc 6-O-sulfotransferase family of enzymes (GST family) is present in H4 at positions 98474-99661. The enzyme encoded by this long (1188 bp) ORF is predicted to be a typical type two transmembrane protein of 395 amino acids with 85.6 % identity and 87.4 % similarity on the amino acid level. The putative gene product was therefore termed [GST-4□] GST-4α to highlight its similarity to GST4 the latter being referred to henceforth as [GST-4□] GST-4β. In order to address the question, whether [GST-4□] GST-4β is being expressed in vivo, we searched the Genbank and LifeSeq EST database for matching expressed sequence tags (ESTs). We found two matching ESTs (accession number AI824100 from Genbank, and clone #6869651 from LifeSeq). Plasmids containing both sequences were retrieved and sequenced in full. AI824100 was found to contain the [GST-4□] GST-4β ORF from its start ATG through a Not I site (GCGGCCGC) at position 795 of this ORF. In addition, this plasmid contained 188 bases of [GST4□] GST-4β 5'UTR. Incyte clone #6869651 contained the [GST-4□] GST-4β ORF from the Not I site at position 795 of the ORF through the stop-codon (TAG) and additional 307 bp of 3'UTR. A [GST4□] GST-4β cDNA constructed from these two ESTs is presented in sequence 3. This sequence was mapped back against the contig H4. It was thus found that the [GST4□] GST-4β ORF along with 17 bp of 5'UTR and all of the 3'UTR were contained within a single exon located within H4 at positions 98457-99968 (commencing 50.5 kb downstream from the start of the [GST-4□] GST-4α ORF). The [GST4□] GST-4β 5'UTR was again contained in at least two small exons located upstream of the [GST-4b] GST-4β ORF but downstream of the [GST-4□] GST-4α ORF. Thus 4b_5U1 (bases 100 - 171 in [GST4□] GST-4β cDNA, sequence 3) corresponds to bases 96413-96484 in the contig. And 4b_5U2 (bases 9 - 99 in [GST4□] GST-4β cDNA) corresponds to bases 83257-83347 in the contig. 5' regulatory sequences controlling the transcription of [GST4□] GST-4β gene in the cell (GST-4 promoter) may be located somewhere upstream of 4b_5U2 but downstream of the [GST4□] GST-4α ORF and/or transcription of [GST4□] GST-4α and [-□] -β may be controlled by common regulatory sequences. Thus, as shown schematically in Figure 7, the H4 gene is actually a tandem repeat of two highly similar *GST* genes [*GST4*□] *GST4α* and [*GST4*□] *GST4β*. The enzyme encoded by [*GST4*□] *GST4α* has been shown experimentally to catalyze 6-O-sulfation at GlcNAc in mucin-type acceptor glycoproteins (GlyCAM-1). [GST-4□] GST-4β is 85.6 % identical to [GST-4□] GST-4α [(] on the amino acid level.

IN THE CLAIMS

Please enter the amendments to claims 5-8 and 12, as shown below.

5. (Amended) A nucleic acid present in other than its natural environment, wherein said nucleic acid [has] comprises a nucleotide sequence encoding a [glycosyl sulfotransferase according to Claim 1] glycosyl sulfotransferase-4α (GST-4α) polypeptide, wherein said GST-4α polypeptide comprises an amino acid sequence that is at least 85% identical to the amino acid sequence set forth in SEQ ID NO:08.

7. (Amended) A nucleic acid according to Claim 5, wherein said nucleic acid [has] comprises a nucleic acid sequence that is substantially identical to or the same as the nucleotide sequence of SEQ ID NOS: 01, 02, 03, 04, [05, 06] 10, or 11 [12, 18, or 19].

7. (Amended) A fragment of the nucleic acid according to Claim 5, wherein said fragment catalyzes the transfer of a sulfate group from a donor to a selectin ligand.

8. (Amended) An isolated nucleic acid [or mimetic thereof] that hybridizes [under stringent conditions] at 50°C or higher in a solution of 15 mM NaCl and 1.5 mM sodium citrate to the nucleic acid according to Claim [5] 6 or [its] a complementary sequence thereof, wherein said nucleic acid encodes a glycosyl sulfotransferase.

9. (Amended) An expression cassette comprising a transcriptional initiation region functional in an expression host, a nucleic acid [having] comprising a nucleotide sequence found in the nucleic acid according to Claim 5 or claim 7 under the transcriptional regulation of said transcriptional initiation region, and a transcriptional termination region functional in said expression host.

12. (Amended) A method of producing a glycosyl sulfotransferase [according to Claim 1], said method comprising:

growing a cell according to Claim 10, whereby said glycosyl sulfotransferase is expressed; and

isolating said glycosyl sulfotransferase substantially free of other proteins.